Poster I-41

Exploiting Self-Assembly of Cells and Tissues To Build Biological Structures of Prescribed Shape

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Self-assembly is a fundamental process, which drives structural organization in both inanimate and living systems. It is in the course of self-assembly of cells and tissues in early development that the organism and its parts eventually acquire their final shape. Even though developmental patterning through self-assembly is under strict genetic control it is clear that physical mechanisms must underline the formation of complex structures. Here we show both experimentally and using computer simulations how tissue liquidity can be employed to build tissue constructs of prescribed geometry in vitro. Cell aggregates, which consist of many thousand cells and form spheres, were implanted contiguously into biocompatible hydrogels in circular and square geometry. Depending on the properties of the gel, upon incubation the aggregates either fused into toroidal or planar three-dimensional structure or their constituent cells dispersed into the surrounding matrix. The model simulations reproduced the experimentally observed shapes and revealed that the control parameter of structure formation is the aggregate-gel interfacial tension. The model-based analysis also revealed that the observed toroidal structure represents a metastable state of the cellular system whose lifetime depends on the magnitude of cell-cell and cell-matrix interactions. Thus, fine tuning of control parameters assures the stability of these constructs over a long time. We suggest that spherical aggregates composed of organ-specific cells may be used as “bioink” in the evolving technology of organ printing.